

**PATENT****IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Application of:

SKOULTCHI

Serial No.: 08/102,390

Group Art Unit: 1804

Filed: August 5, 1993

Examiner: Ziska, S.

For: PRODUCTION OF PROTEINS  
USING HOMOLOGOUS  
RECOMBINATION

Atty Docket No.:  
7639-017/Cell 3.2

DECLARATION OF LAURA A. CORUZZI

Honorable Commissioner of Patents and Trademarks  
Washington, D.C. 20231

Sir:

I, Laura A. Coruzzi, declare that:

1. I am a registered patent attorney (Registration No. 30,742), and Attorney for Applicant of the above-identified patent application. I make this declaration in support of Applicant's Petition To Make Special Pursuant To 37 C.F.R. §1.102(d), filed concurrently herewith.

2. I have read and am familiar with:

- (a) a Declaration of Daniel J. Capon (the "Capon Declaration") filed concurrently herewith;
- (b) an S-1 Registration Statement by Transkaryotic Therapies, Inc. ("TKT") filed with the Securities and Exchange Commission on July 26, 1993, pertinent pages of which are attached to the Capon Declaration as Exhibit B;
- (c) a published report entitled "TKT Scientists Deliver Erythropoietin (EPO) By Gene Therapy; Novel Gene Activation Technology Eliminates Need For EPO License" which appeared in PR Newswire's "Today's Headlines" on January 12, 1994,

attached to the Capon Declaration as Exhibit C; and

- (d) a published report entitled "Mice Produce EPO In Gene Therapy Study" which appeared in BioWorld Today, Vol.5, No. 9, pp. 1-2, on January 13, 1994, attached to the Capon Declaration as Exhibit D.

3. I have also read and am familiar with the claims as amended in an Amendment Under 37 C.F.R. §1.115, filed on June 1, 1994, in the above-identified patent application.

4. I have made a "rigid comparison" of TKT's gene activation technology and the amended claims of this application, using the description of TKT's gene activation technology presented in Exhibits B-D of the Capon Declaration and Dr. Capon's opinion of what that description means [Capon Declaration, §§ 10 and 11]. On the basis of that comparison, I believe that some of the claims of this application are unquestionably infringed.

For example, I have made a "comparison" with respect to amended claim 26. I believe that TKT's gene activation technology "unquestionably" infringes such claim because TKT's gene activation technology produces mammalian host cells having a modified endogenous gene comprising a nucleotide regulatory element different from the wild-type regulatory element normally associated with the endogenous gene [Capon Declaration, § 10(c)-(e)], in which:

- a) the different regulatory element is integrated into the genome of the mammalian host cell via homologous recombination [Capon Declaration, § 10(b)];

b) the integrated regulatory element is operatively associated with the endogenous gene of the mammalian host cell [Capon Declaration, ¶ 10(e)]; and

c) expression of the endogenous gene is controlled by the integrated regulatory element [Capon Declaration, ¶ 10(e)].

5. I have also made a "comparison" with respect to amended claim 48. I believe that TKT's gene activation technology "unquestionably" infringes such claim because TKT's gene activation technology is a method for producing a mammalian host cell having a modified gene, comprising:

a) transforming a mammalian host cell with a nucleotide sequence comprising a nucleotide regulatory element flanked by a nucleotide sequence homologous to a region of the host cell genome within or proximal to an endogenous gene present in the mammalian host cell so that the nucleotide regulatory element is integrated via homologous recombination into the genome of the mammalian host cell [Capon Declaration, ¶¶ 10, 11]; and

b) selecting a transformed mammalian host cell having the modified gene in which the integrated nucleotide regulatory element is operatively associated with the endogenous gene so that expression of the endogenous gene is controlled by the integrated regulatory element [Capon Declaration, ¶ 10(e), (f)].

6. I have a "good knowledge of the pertinent prior art" and believe that all of the claims in the application are

allowable. The Examiner in charge of Applicant's application cited several documents during her examination (see, for example, Paper No. 11, mailed September 21, 1994). Applicant also submitted an Information Disclosure Statement Under 37 C.F.R. §1.56 on November 9, 1993, and a Supplemental Information Disclosure Statement on June 1, 1994.

I have reviewed all of these documents and believe that all of the amended claims now pending in this application are patentable over them.

7. The undersigned declares further that all statements made herein of her own knowledge are true, that all statements made on information and belief are believed to be true, and further that these statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such wilful false statements may jeopardize the validity of this application or any patent issuing thereon.

Date: Dec 28, 1994

Laura A. Coruzzi 30,742  
Laura A. Coruzzi (Reg. No.)

ATTORNEY FOR APPLICANT

PENNIE & EDMONDS  
1155 Avenue of the Americas  
New York, New York 10036  
(212) 790-9090